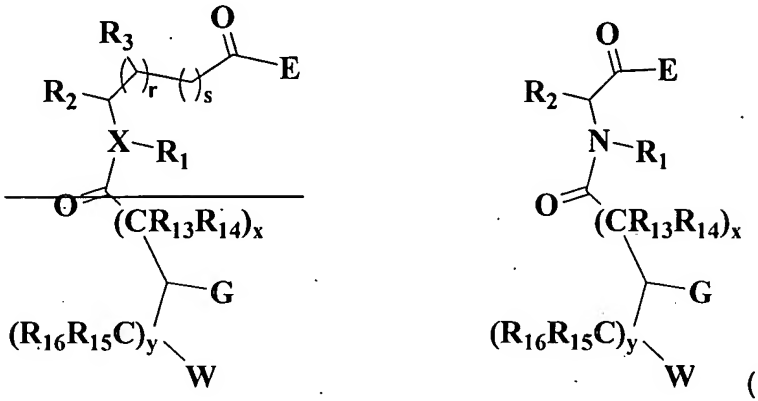
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

1. (Currently Amended) A compound of formula (I),



(I),

or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which:

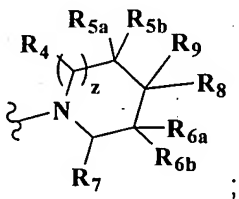
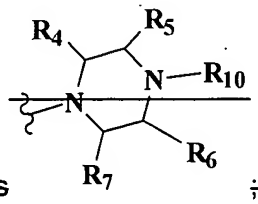
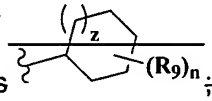
~~X is N or CH;~~

R_1 is hydrogen or C_{1-6}alkyl or is taken together with R_2 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R_2 is ~~hydrogen, aryl, cycloalkyl, heteroaryl, or heterocycle; or~~ C_{1-6}alkyl or C_{2-6}alkenyl optionally substituted with one to three ~~of hydroxy, alkoxy, halogen, cyano, trifluoromethyl, nitro, amino, alkylamino,~~ aryl, cycloalkyl, or heteroaryl[;], ~~and/or heterocycle; or R_2 is taken together with R_1 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;~~ provided that where G is C_{2-6}alkenyl, A_1–$NR_{18}CO_2R_{19}$, or A_1–SO_2R_{17}, or when y is 0, R_2 may be or C_{1-6}alkyl or C_{2-6}alkenyl, each optionally substituted with heteroaryl;

~~R_3 is hydrogen or C_{1-6}alkyl or is taken together with R_2 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;~~

E is ~~E_1, E_2, E_3 or E_4, wherein~~

~~E_1 is~~  ; ~~E_2 is~~  ; ~~E_3 is~~  ; ~~and~~

~~E_4 is $NR_{11}R_{12}$;~~

G is selected from ~~C_{2-6}alkenyl~~, A_3-aryl, $-OR_{18}$, heteroaryl, A_1-cyano, A_2-OR_{17}, $A_1-C(=O)R_{18}$, $A_1-CO_2R_{18}$, $A_1-C(=O)NR_{18}R_{19}$, $A_1-OC(=O)R_{18}$, $A_1-NR_{18}C(=O)R_{19}$, $A_1-OC(=O)NR_{18}R_{19}$, ~~$A_1-NR_{18}CO_2R_{19}$~~, $A_1-NR_{18}SO_2R_{17}$, ~~$A_1-SO_2R_{17}$~~, $A_1-NR_{20}C(=O)NR_{18}R_{19}$, and A_1-SR_{18}; or when *y* is 0, or when W is a group other than NHR_{22}, G may be A_1-heterocyclo, wherein A_1 is a bond, C_{1-6}alkylene or C_{2-6}alkenylene (straight or branched chain), A_2 is C_{1-6}alkylene or C_{2-6}alkenylene, and A_3 is C_{2-6}alkenylene; or where G is C_{2-6}alkenyl, $A_1-NR_{18}CO_2R_{19}$, or $A_1-SO_2R_{17}$, or when y is 0, R_2 may be C_{1-6}alkyl or C_{2-6}alkenyl, each substituted with heteroaryl;

W is selected from $-NR_{21}R_{22}$, $-OR_{23}$, $-NR_{21}C(=O)R_{24}$, $-NR_{21}CO_2R_{24}$, amidino, guanidino, or a substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl selected from azepinyl, azetidinyl, imidazolyl, imidazolidinyl, pyrazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, pyranyl, tetrahydropyranyl, piperazinyl, homopiperazinyl, pyrrolyl, pyrrolidinyl, piperidinyl, thiazolyl, tetrahydrothiazolyl, thienyl, furyl, tetrahydrofuryl, morpholinyl, isoquinolinyl, tetrahydroisoquinolinyl, tetrazolyl, oxazolyl, tetrahydro-oxazolyl, and C_{3-7}cycloalkyl, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have joined thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring;

R_4 and R_7 are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, and keto;

R_5, R_{5a}, R_{5b}, R_6, R_{6a}, R_{6b}, R_8 and R_9 are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, $-OR_{25}$, $-NR_{25}R_{26}$, $-SR_{25}$ $-S(O)_pR_{26}$, $-C(=O)R_{25}$, $-OC(=O)R_{25}$, $-CO_2R_{25}$, $-C(=O)NR_{25}R_{26}$, $-NR_{25}C(=O)R_{26}$, $-OC(=O)NR_{25}R_{26}$, $-NR_{25}CO_2R_{26}$, $-NR_{27}C(=O)NR_{25}R_{26}$ or $-NR_{25}SO_2R_{26}$; or R_{5a} and R_{5b}, R_{6a} and R_{6b}, or R_8 and R_9 taken together form a keto group (=O) or a monocyclic or bicyclic cycloalkyl or heterocyclo joined in a spiro fashion to ring E, or alternatively, R_{5a} and/or R_{5b} together with R_8 and/or R_9, or R_{6a} and/or R_{6b} together with R_8 and/or R_9, are taken to form a fused carbocyclic, heterocyclic, or heteroaryl ring; provided that, when G is a C_{1-6}alkyl substituted with $-OR_{17}$, $-CO_2R_{18}$, or $-C(=O)NR_{18}R_{19}$, then R_{5a}, R_{5b}, R_{6a}, and R_{6b} are hydrogen provided R_8 and R_9 are not both hydrogen;

R_{10} is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and hetereocyclo;

R_{11} is hydrogen or C_{1-8}alkyl;

R_{12} is C_{1-8}alkyl, substituted C_{1-8}alkyl, or cycloalkyl;

R_{13}, R_{14}, R_{15} and R_{16} are selected independently of each other from hydrogen, alkyl, substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclo, or R_{13} and R_{14}, or R_{15} and R_{16}, when attached to the same carbon atom, may join to form a spirocycloalkyl ring;

R_{17} is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, or $C(=O)R_{28}$; or when G is $NH(C=O)R_{19}$, R_{19} may be a bond joined to W to define a heterocyclo ring; provided, however, that when *y* is at least one, W is imidazolyl, indolyl, $-NR_{21}R_{22}$, or $-OR_{23}$, and G is $-NR_{18}C(=O)R_{19}$, then R_{19} is not a C_1-alkyl having the substituent $-NR_{29}R_{31}$;

R_{21} and R_{22} are selected from hydrogen, alkyl, and substituted alkyl;

R_{23} and R_{24} are independently hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

R_{25}, R_{26} and R_{27} are independently hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or R_{25} and R_{26} may join together to form a heterocyclo or heteroaryl, except R_{26} is not hydrogen when joined to a sulfonyl group as in $-S(O)_pR_{26}$ or $-NR_{25}SO_2R_{26}$;

R_{28} is hydrogen, alkyl, or substituted alkyl;

R_{29} and R_{31} are selected from hydrogen, alkyl, haloalkyl, hydroxyalkyl, phenylalkyl, and alkoxycarbonylalkyl, or R_{29} and R_{31} taken together form a heterocyclo ring;

n is 0, 1, 2, 3 or 4;

p is 1, 2, or 3;

~~*r* and *s* are 0 or 1;~~

x is 0, 1, or 2;

y is 0, 1, 2, 3 or 4; and

z is 0, 1, or 2.

2. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] <u>or</u> hydrate, ~~or prodrug~~ thereof, in which:

, in which:

G is selected from:

~~a) C_{2-4}alkenyl optionally substituted with phenyl;~~

a[b]) $-CO_2R_{18}$, $-C(=O)NR_{18}R_{19}$, $-NR_{18}C(=O)R_{19}$, and $-SO_2R_{17}$,

b[c]) C_{1-6}alkylene or C_{2-6}alkenylene joined to one of cyano, $-OR_{17}$, $-C(=O)R_{18}$, $-CO_2R_{18}$, $-C(=O)NR_{18}R_{19}$, $-NR_{18}C(=O)R_{19}$, $-NR_{18}CO_2R_{19}$, $-NR_{18}SO_2R_{17}$, $-SO_2R_{17}$, $-NR_{20}C(=O)NR_{18}R_{19}$, and $-SR_{18}$;

c[d]) ~~when y is 0,~~ or when W is a group other than NHR_{22}, G also may be selected from optionally substituted pyrrolidinyl or piperidinyl;

R_{17} is C_{1-4}alkyl, C_{5-6}cycloalkyl, phenyl or benzyl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, C_{1-4}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, -C(=O)CH_2(phenyloxy), -C(=O)CH_2(benzyloxy), imidazolyl, pyridyl, furyl, thienyl, or C_{1-4}alkyl or C_{2-4}alkenyl substituted with one of phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl, CO_2Me, phenyloxy, or benzyloxy, wherein each ringed group of R_{18}, R_{19}, and R_{20} in turn is optionally substituted with one to two R_{36}, and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto; and

R_{36} is halogen, methoxy, nitro, phenyl, phenyloxy, or alkylamino.

3. (Currently Amended) A compound according to claim 2, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

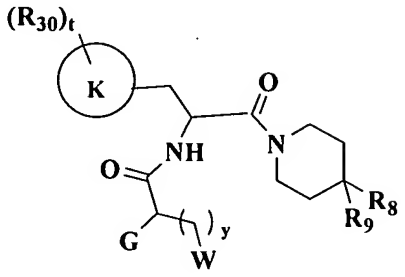
G is $-NR_{18}C(=O)R_{19}$,

R_{18} is hydrogen or lower alkyl, and

R_{19} is C_{1-4}alkyl, C_{2-4}alkenyl, phenyl, benzyl, C_{5-6}cycloalkyl, -C(=O)CH_2(phenyloxy), -C(=O)CH_2(benzyloxy), imidazolyl, pyridyl, furyl, thienyl, or C_{1-4}alkyl or C_{2-4}alkenyl substituted with one of phenyl, phenyl, pyridyl, furyl, cyclopentyl, cyclohexyl, CO_2Me, phenyloxy, and benzyloxy, wherein each ringed group of R_{19} in turn is optionally substituted with one to two R_{36}, and/or optionally has a benzene ring or five membered heterocyclo having two oxygen atoms fused thereto.

4. (Currently Amended) A compound according to claim 2, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which W is OH, $-NH_2$, -NHalkyl, $-N(alkyl)_2$, azetidinyl, imidazolyl, piperidinyl, pyrrolidinyl, or $NHCO_2$(alkyl); or a C_{4-7}cycloalkyl optionally substituted with lower alkyl, $-NH_2$, -NHalkyl, or $-N(alkyl)_2$.

5. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, having the formula:



in which

K is phenyl or thiazolyl;

R_{30} is selected from C_{1-4}alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and –C(=O)phenyl;

t is 0, 1 or 2; and

y is 0, 1 or 2.

6. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

W is OH, $-NR_{21}R_{22}$, $-NHC(=O)R_{24}$, or $-NHCO_2$alkyl;

R_{21} and R_{22} are independently selected from hydrogen, C_{1-8}alkyl, and $(CH_2)_q$-J, wherein J is selected from napthyl, furanyl, indolyl, imidazolyl, pyrimidinyl, benzothienyl, pyridinyl, pyrrolyl, pyrrolidinyl, thienyl, and C_{3-7}cycloalkyl, wherein the alkyl, alkylene, and/or J groups of R_{21} and/or R_{22} are optionally substituted with up to three R_{33};

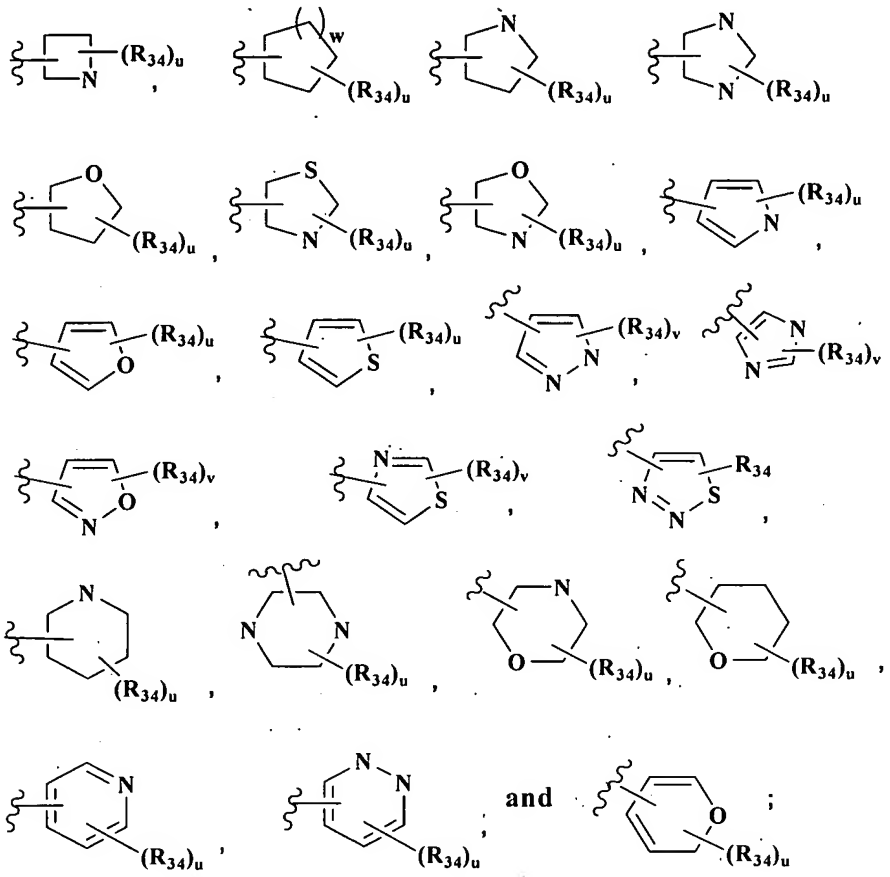
R_{24} is selected from C_{1-6}alkyl, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrollylalkyl, piperidinyl, and piperidinylalkyl, wherein R_{24} in turn is optionally substituted with one to two C_{1-4}alkyl and/or $-CO_2(C_{1-4}$alkyl);

R_{33} is selected from C_{1-6}alkyl, hydroxy, C_{1-4}alkoxy, amino, C_{1-4}alkylamino, aminoC_{1-4}alkyl, trifluoromethyl, halogen, phenyl, benzyl, phenyloxy, benzyloxy, $-C(=O)(CH_2)NH_2$, $-CO_2(C_{1-4}$alkyl), $-SO_2(C_{1-4}$alkyl), tetrazolyl, piperidinyl, pyridinyl, and indolyl, wherein when R_{33} includes a ring, said ring in turn is optionally substituted with one to two C_{1-4}alkyl, hydroxy, methoxy, and/or halogen; and

q is 0, 1, 2 or 3.

7. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

W is a ring selected from:



R_{34} at each occurrence is attached to any available carbon or nitrogen atom of W and is selected from C_{1-6}alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, –C(=O)alkyl, –C(=O)aminoalkyl, –C(=O)phenyl, –C(=O)benzyl, –CO_2alkyl, –CO_2phenyl, –CO_2benzyl, –SO_2alkyl, –SO_2aminoalkyl, –SO_2phenyl, –SO_2benzyl, phenyl, benzyl, phenyloxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and/or two R_{34} when attached to two adjacent carbon atoms or adjacent carbon and nitrogen atoms may be taken together to form a fused benzo, heterocyclo, or heteroaryl ring, and/or two R_{34} when attached to the same carbon atom (in the case of a non-aromatic ring) may form keto (=O), and each R_{34} in turn is optionally substituted with up to two R_{35};

R_{35} is selected from halogen, trifluoromethyl, C_{1-4}alkyl, cyano, nitro, trifluoromethoxy, amino, alkylamino, aminoalkyl, hydroxy, and C_{1-4}alkoxy;

w is selected from 0, 1, or 2;

u is selected from 0, 1, 2, and 3; and

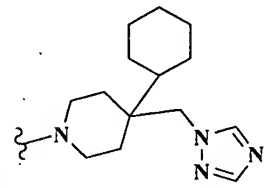
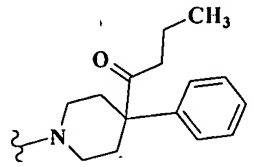
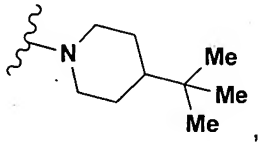
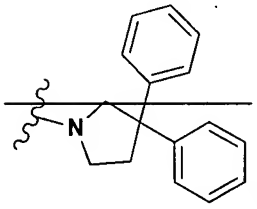
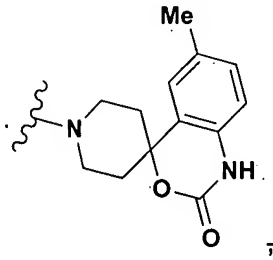
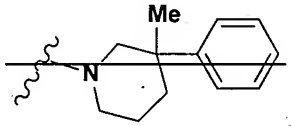
v is 0, 1 or 2.

8. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

R_8 and R_9 are selected independently from hydrogen, alkyl, $-(CH_2)_j$-C(=O)alkyl, $-(CH_2)_j$-phenyl, $-(CH_2)_j$-napthyl, $-(CH_2)_j$-C_{4-7}cycloalkyl, $-(CH_2)_j$-heterocyclo, and $-(CH_2)_j$- heteroaryl, provided R_8 and R_9 are not both hydrogen, or R_8 and R_9 together form a spirocycloalkyl or spiroheterocyclic ring; and

j is selected from 0, 1, 2 and 3.

9. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

E is  ,  ,  ,  or  , ~~or~~ 

10. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

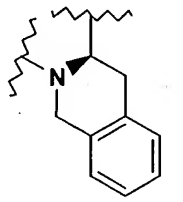
R_2 is selected from ~~hydrogen~~, C_{1-6}alkyl, C_{2-6}alkenyl~~, biphenyl~~, C_{2-6}alkenylene-K, and $-(CH_2)_g$-K;

K is selected from phenyl, napthyl, thienyl, thiazolyl, pyridinyl, pyrimidinyl, and C_{5-6}cycloalkyl, wherein each group K in turn is optionally substituted with one to three R_{30} or has a benzene ring fused thereto, which also may be substituted with one to three R_{30};

R_{30} is selected from C_{1-4}alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and acylphenyl; and

g is 0, 1, 2 or 3.

11. (Withdrawn) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which $-X(R_1)-CH(R_2)-CH(R_3)_r-(CH_2)_s-$, taken together are selected from C_{1-4}alkylene,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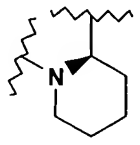
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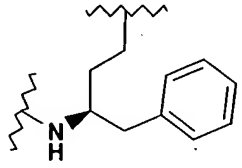
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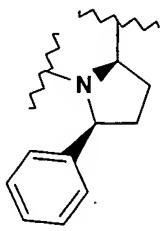
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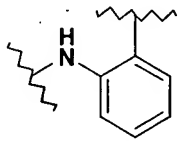
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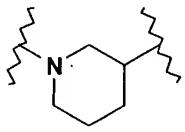
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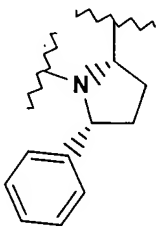
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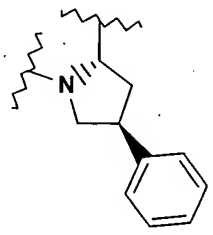
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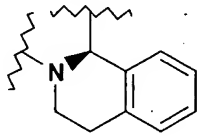


12. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which

~~X is N;~~

R_1 is hydrogen or C_{1-4}alkyl[;]

~~r is 0; and~~

~~s is 0.~~

13. (Canceled) A compound according to claim 1, or a pharmaceutically-acceptable salt hydrate, or prodrug thereof, in which

G is C_{2-4}alkenyl, $NHC(=O)R_{19}$, SO_2R_{17}, or when y is 0, G may also be pyrrolidinyl, piperidinyl, pyrrolidinyl(lower alkyl), or piperidinyl(lower alkyl);

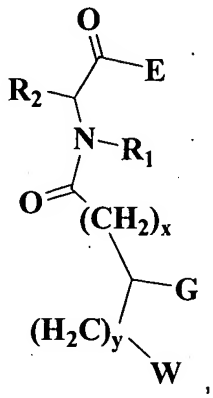
W is $-NR_{21}R_{22}$, $NR_{21}C(=O)R_{24}$, azetidinyl, or imidazolyl;

R_{17} and R_{19} are lower alkyl, and when W is imidazolyl, R_{19} may be joined with W to form a heterocycle;

R_{21} and R_{22} are selected from hydrogen and lower alkyl; and

y is 0, 1, or 2.

14. (Currently Amended) A compound having the formula,



or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which:

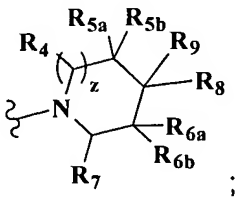
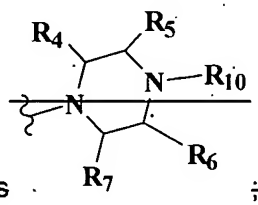
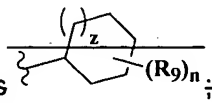
~~X is N or CH;~~

R_1 is hydrogen or C_{1-6}alkyl or is taken together with R_2 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;

R_2 is ~~hydrogen, aryl, cycloalkyl, heteroaryl, or heterocyclo; or~~ C_{1-6}alkyl or C_{2-6}alkenyl optionally substituted with one to three ~~of hydroxy, alkoxy, halogen, cyano, trifluoromethyl, nitro, amino, alkylamino,~~ aryl, cycloalkyl, or heteroaryl[;], ~~and/or heterocyclo~~; ~~or R_2 is taken together with R_1 or R_3 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;~~ provided that where G is C_{2-6}alkenyl, A_1–$NR_{18}CO_2R_{19}$, or A_1–SO_2R_{17}, or when y is 0, R_2 may be or C_{1-6}alkyl or C_{2-6}alkenyl, each optionally substituted with heteroaryl;

~~R_3 is hydrogen or C_{1-6}alkyl or is taken together with R_2 to form a monocyclic or bicyclic aryl, cycloalkyl, heteroaryl or heterocycle;~~

E is ~~E_1, E_2, E_3 or E_4, wherein~~

~~E_1 is~~  ; ~~E_2 is~~  ; ~~E_3 is~~  ; ~~and~~

~~E_4 is $NR_{11}R_{12}$;~~

G is selected from:

~~a) C_{2-4}alkenyl optionally substituted with phenyl;~~

a[b]) $-CO_2R_{18}$, $-C(=O)NR_{18}R_{19}$, $-NR_{18}C(=O)R_{19}$, and $-SO_2R_{17}$,

b[c]) C_{1-6}alkylene or C_{2-6}alkenylene joined to one of cyano, $-OR_{17}$, $-C(=O)R_{18}$, $-CO_2R_{18}$, $-C(=O)NR_{18}R_{19}$, $-NR_{18}C(=O)R_{19}$, $-NR_{18}CO_2R_{19}$, $-NR_{18}SO_2R_{17}$, $-SO_2R_{17}$, $-NR_{20}C(=O)NR_{18}R_{19}$, and $-SR_{18}$;

c[d]) ~~when y is 0,~~ or when W is a group other than NHR_{22}, G also may be selected from optionally substituted pyrrolidinyl or piperidinyl;

W is selected from $-NR_{21}R_{22}$, $-OR_{23}$, $-NR_{21}C(=O)R_{24}$, $-NR_{21}CO_2R_{24}$, amidino, guanidino, or a substituted or unsubstituted heterocyclo, heteroaryl, or cycloalkyl group selected from azetidinyl, imidazolyl, imidazolidinyl, pyrazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, pyranyl, tetrahydropyranyl, piperazinyl, homopiperazinyl, pyrrolyl, pyrrolidinyl, piperidinyl, thiazolyl, tetrahydrothiazolyl, thienyl, furyl, tetrahydrofuryl, morpholinyl, isoquinolinyl, tetrahydroisoquinolinyl, tetrazolyl, oxazolyl, tetrahydro-oxazolyl, and C_{3-7}cycloalkyl, wherein said heteroaryl, heterocyclo or cycloalkyl groups may additionally have fused thereto an optionally substituted five-to-seven membered heterocyclic, heteroaryl, or carbocyclic ring;

R_4 and R_7 are independently selected from hydrogen, alkyl, substituted alkyl, halogen, hydroxy, alkoxy, and keto;

R_5, R_{5a}, R_{5b}, R_6, R_{6a}, R_{6b}, R_8 and R_9 are independently hydrogen, halogen, cyano, alkyl, substituted alkyl, alkenyl, hydroxy, alkoxy, alkoxycarbonyl, acyl, cycycloalkyl, heterocyclo, aryl, or heteroaryl; or R_{5a} and R_{5b}, R_{6a} and R_{6b}, or R_8 and R_9 taken together form a keto group (=O) or a monocyclic or bicyclic cycloalkyl or heterocyclo joined in a spiro fashion to ring E, or alternatively, R_{5a} and/or R_{5b} together with R_8 and/or R_9, or R_{6a} and/or R_{6b} together with R_8 and/or R_9, join together to form a fused benzene or heterocyclo ring; provided that, when G is a C_{1-6}alkyl substituted with $-OR_{17}$, $-CO_2R_{18}$, or $-C(=O)NR_{18}R_{19}$, then R_{5a}, R_{5b}, R_{6a}, and R_{6b} are hydrogen;

R_{10} is selected from hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, and hetereocyclo;

R_{11} is hydrogen or C_{1-8}alkyl;

R_{12} is C_{1-8}alkyl, substituted C_{1-8}alkyl, or cycloalkyl;

R_{17} is alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl;

R_{18}, R_{19}, and R_{20} are independently selected from hydrogen, alkyl, alkenyl, aryl, heteroaryl, cycloalkyl, heterocyclo, C(=O)R_{28} or a C_{1-4}alkyl or C_{2-4}alkenyl substituted with one or more of aryl, heteroaryl, cycloalkyl, heterocyclo, alkoxycarbonyl, phenyloxy, and/or benzyloxy, and each of said ringed groups of R_{18}, R_{19}, and R_{20} in turn is optionally substituted with one to two R_{36};

R_{21} and R_{22} are selected from alkyl and substituted alkyl;

R_{23} and R_{24} are independently selected from hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

R_{28} is hydrogen, alkyl, or substituted alkyl;

R_{36} is halogen, methoxy, nitro, phenyl, phenyloxy, or alkylamino;

n is 0, 1, 2, 3 or 4;

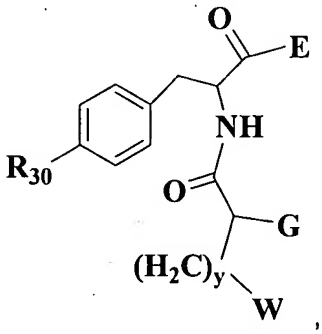
~~*r and s are 0 or 1;*~~

x is 0, 1, or 2;

y is 0, 1, 2, 3 or 4; and

z is 0, 1, or 2.

15. (Canceled) A compound according to claim 14, or a pharmaceutically-acceptable salt hydrate, or prodrug thereof, having the formula:



wherein G is C_{2-4}alkenyl, NHC(=O)R_{19}, SO_2R_{17}, or when y is 0, G may also be pyrrolidinyl, piperidinyl, pyrrolidinyl(lower alkyl), or pipridinyl(lower alkyl);

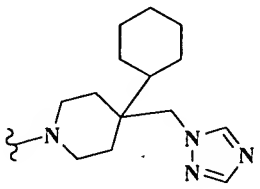
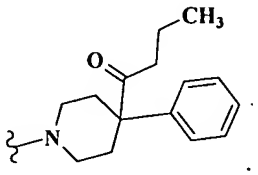
W is OH, $-NH_2$, NH(lower alkyl), N(lower alkyl)$_2$, azetidinyl, or imidazolyl, wherein the azetidinyl and imidazolyl are optionally substituted with lower alkyl;;

R_{17} and R_{19} are lower alkyl or phenyl;

R_{30} is C_{1-4}alkyl, hydroxy, methoxyl, ethoxy, halogen, nitro, cyano, amino, C_{1-4}alkylamino, phenyl, or C(=O)phenyl; and

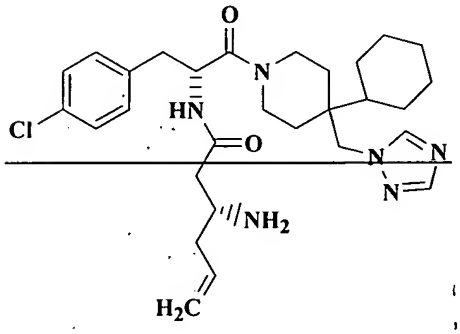
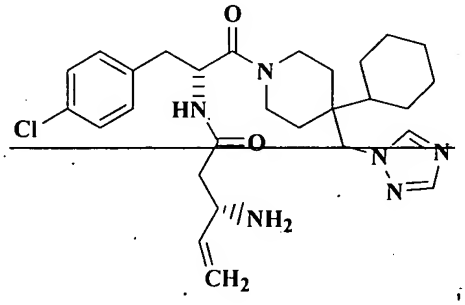
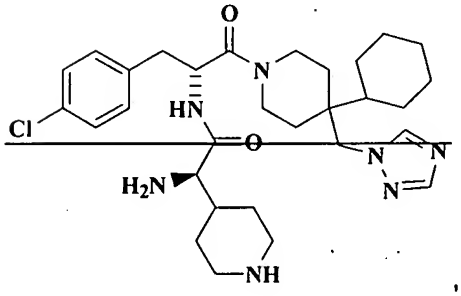
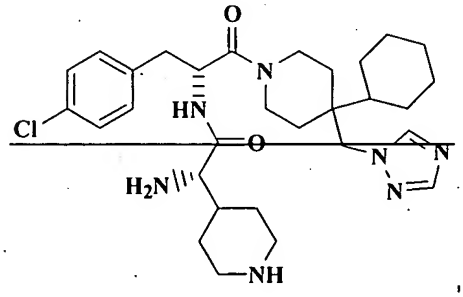
y is 0, 1, or 2.

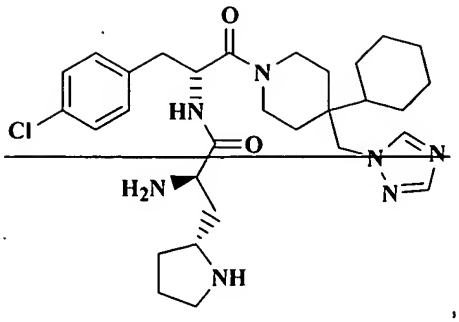
16. (Currently Amended) A compound according to claim 15, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which E is

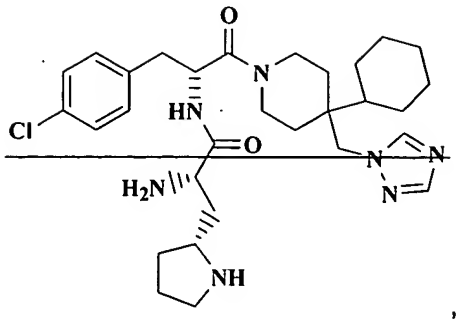

or


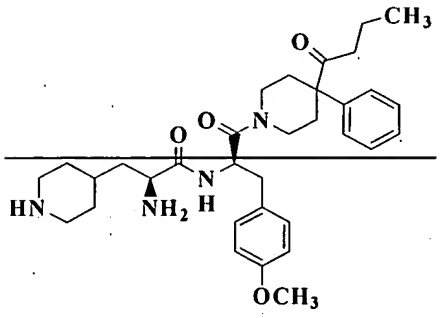
17. (Currently Amended) A compound according to claim 14, or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof, in which G is NHC(=O)(alkyl) or NHC(=O)phenyl.

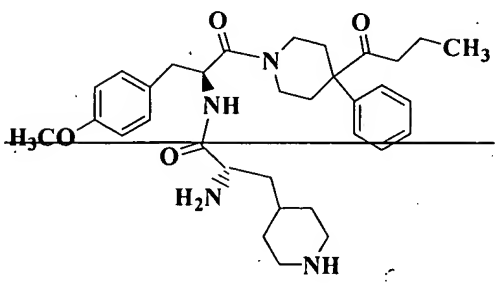
18. (Currently Amended) A compound according to claim 1, having the formula,

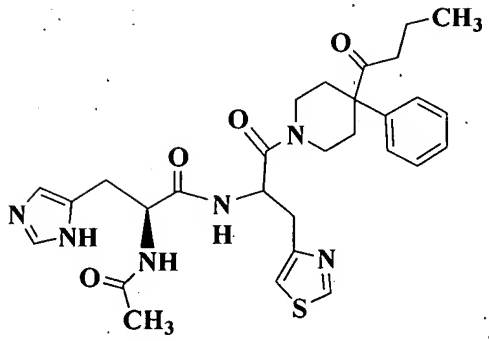





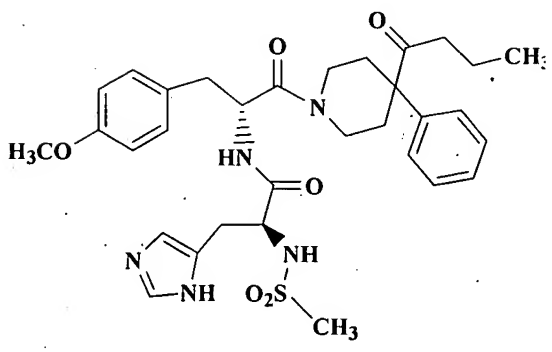


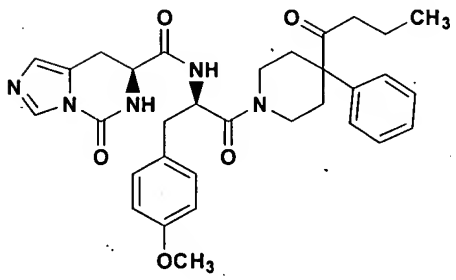


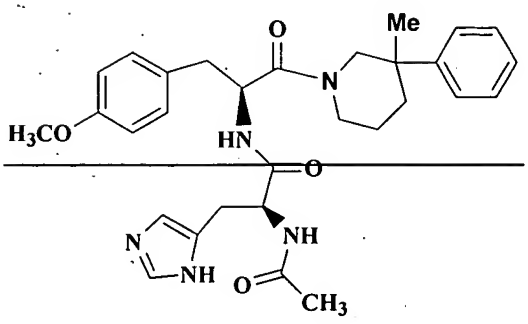


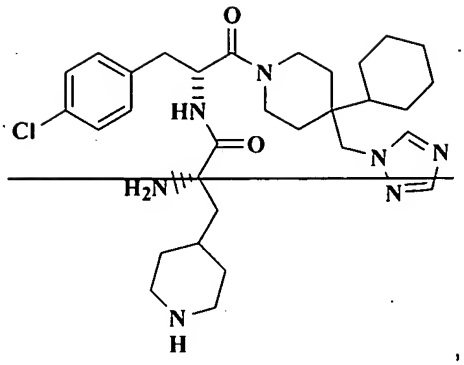


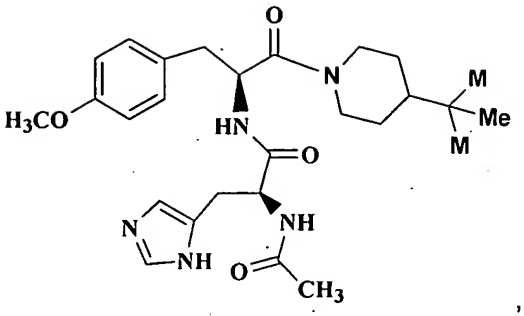


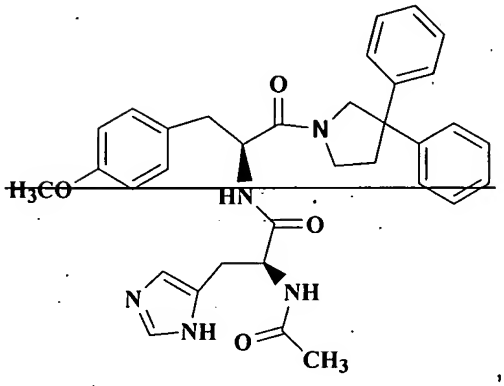


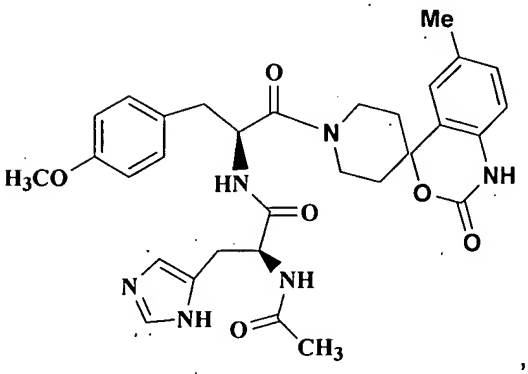












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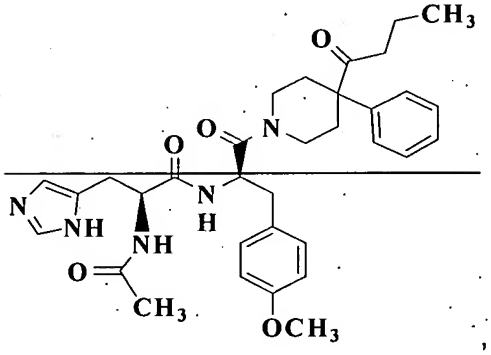

or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof.

19. (Currently Amended) A pharmaceutical composition comprising at least one compound according to claim 1 or a pharmaceutically-acceptable salt[,] or hydrate, ~~or prodrug~~ thereof; and a pharmaceutically-acceptable carrier or diluent.

20. (Withdrawn) A pharmaceutical composition comprising (i) at least one compound according to claim 1 or a pharmaceutically-acceptable salt hydrate, or prodrug thereof; (ii) at least one second

compound effective for treating an inflammatory or immune disease, a cardiovascular disease, or a neurodegenerative condition; and (iii) a pharmaceutically-acceptable carrier or diluent.

21. (Withdrawn) The pharmaceutical composition according to claim 20 in which the at least one second compound comprises a phosphodiesterase inhibitor.

22. (Withdrawn) A method of treating a melanocortin-receptor associated condition, the method comprising administering to a warm-blooded species in need of such treatment a therapeutically-effective amount of at least one compound according to claim 1.

23. (Withdrawn) The method of claim 22 in which the melanocortin-receptor associated condition is an MC-1R or MC-4R condition.